Complete Summary

GUIDELINE TITLE

Interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of chronic hepatitis C.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of chronic hepatitis C. London (UK): National Institute for Clinical Excellence (NICE); 2004 Jan. 38 p. (Technology appraisal; no. 75).

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Chronic hepatitis C

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine

INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To assess the clinical and cost-effectiveness of interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of chronic hepatitis C

TARGET POPULATION

Patients aged 18 years and over with moderate to severe chronic hepatitis C (CHC)

INTERVENTIONS AND PRACTICES CONSIDERED

1. Peginterferon alfa and ribavirin combination therapy
2. Peginterferon alfa monotherapy

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness (sustained clearance of infection, as shown by absence of viral RNA 6 months or longer after the end of treatment; adverse effects of treatment)
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the Southampton Health Technology Assessment Centre (SHTAC) (see the "Companion Documents" field).

Inclusion Criteria:

The following inclusion criteria, as specified in the study protocol, were set:

Interventions

- Dual therapy (pegylated interferon alpha and ribavirin) versus dual therapy (interferon alpha and ribavirin)
- Monotherapy (pegylated interferon alpha) versus monotherapy (interferon alpha)

Patients

- For the primary research question on the effectiveness of pegylated interferon treatment the patient group were those with moderate to severe chronic hepatitis C infection not previously treated with interferon alpha.
- The protocol for the review also mentions the possible extension of the scope to include patients with chronic mild disease. However, results of a key trial of anti-viral therapy in mild disease are not yet available. Consequently, the focus is primarily on patients with more advanced disease.
- For the secondary research question on re-treatment, the patients of interest were those who had previously failed interferon alpha monotherapy and were being re-treated with dual therapy (interferon alpha and ribavirin).
- Patients with acute hepatitis C were not included in the current report, however, a brief summary of evidence for the effectiveness of anti-viral treatment in this area is provided in section 3.8 of the assessment report.

Outcome Measures (for clinical-effectiveness studies)

- Sustained clearance of infection, as shown by absence of viral RNA 6 months or longer after the end of treatment
- Adverse effects of treatment

Study Types

- Clinical-effectiveness of treatment: systematic reviews (including meta-analyses) of randomised controlled trials (RCTs); and Phase III RCTs
- Cost-effectiveness: cost-effectiveness/cost-utility studies; quality of life studies

Publication Status

- Fully published peer-reviewed reports/articles were used for primary analysis.
- Unpublished material (including conference abstracts) was used primarily for background information and context. Where relevant, studies reported in conference abstract form are summarised in the current report but their results are not used in economic modelling (although they potentially could be used in sensitivity analysis), or to support conclusions or recommendations. Caveats are included to urge caution in the interpretation of such material. See Appendix 4 of the assessment report for a table of conference abstracts of pegylated interferon treatment.

- Material supplied as academic or commercial in confidence is underlined in the current report.

Language

- Only English language articles were included.

Literature Searching

A sensitive search strategy was developed, tested, and refined by an information scientist in order to capture the range of relevant study types (see Appendix 2 of the assessment report for search strategy). The strategy was applied to the following electronic bibliographic databases:

- Medline (Silverplatter)
- Pre-Medline (PubMed)
- Embase (Silverplatter)
- Cochrane Database of Systematic Reviews (CDSR)
- Cochrane Controlled Trials Register (CCTR)
- BIOSIS
- Web of Science Proceedings
- Science Citation Index (SCI)
- Database of Abstracts of Reviews (DARE)
- National Health Service (NHS) Centre for Reviews and Dissemination (CRD) Health Technology Assessment (HTA) database (University of York)
- NHS Economic Evaluation Database (NEED)
- National Research Register (NRR)

Searches were run for the period 2000 to August/September 2002. In March 2003 these were repeated to identify any studies published since September 2002. Searching for studies of re-treatment to interferon monotherapy followed a slightly different method and full details are provided in section 3.3 of the assessment report.

Contact was made with experts in the field to identify relevant trials, and internet sites listing details of current controlled trials and those dealing with hepatitis and liver disease were also searched. The submissions to NICE from the drug companies were also used as a method of identifying relevant studies.

References to studies identified through literature searching were downloaded into Reference Manager software. Inclusion criteria were applied to titles and abstracts and, where necessary, full reports were retrieved for further inspection. A keywording classification system for the database was devised, tested, and refined. The purpose was to facilitate efficient retrieval from the database of relevant studies. A keyword was applied to each record in the database to indicate whether it was to be included or excluded. Further keywords were applied to included studies to indicate study type (e.g. clinical-effectiveness; cost effectiveness; epidemiology etc). Clinical-effectiveness studies were further classified according to the nature of the intervention (e.g. PEG dual therapy); the study type (e.g. randomized controlled trial [RCT]); and whether or not any additional relevant information was provided (e.g. an integral cost effectiveness analysis).

NUMBER OF SOURCE DOCUMENTS

Initial literature searching generated a total of 637 'hits' (i.e. references to studies). As the review progressed 198 references were added to the database most of which had been identified through searching reference lists of papers already retrieved. At the end of March 2003 the original literature search was repeated to identify studies published since the original search. A further 159 references were added to the database, bringing the grand total of articles identified to 996.

A total of 6 fully published RCTs of the effectiveness of pegylated interferon treatment met the inclusion criteria for review (Please refer to section 3.5 of the assessment report for full details of the number of re-treatment studies identified).

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Randomized Controlled Trials
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Data Extraction and Critical Appraisal

Included clinical-effectiveness studies of pegylated interferon treatment underwent detailed data extraction to a standardised template. Studies were also critically appraised using criteria devised by the National Health Services Centre for Review and Dissemination (NHS CRD) (see Appendix 5 of the assessment report).

Extraction and appraisal were performed by one reviewer and checked by a second with disagreements resolved through discussion.

Methods of Analysis/Synthesis

Both qualitative and quantitative approaches were employed to synthesise the results of the randomised controlled trials (RCTs). Data extraction tables were used to compile a narrative summary of the main characteristics and results of the trials. In addition, a meta-analysis was performed with Cochrane Review Manager Software (Version 4.1) using a random effects model.

'Confidence Interval Analysis' software (Version 0.2, © Gardner, 1989) was used to compute confidence intervals where not provided by study authors.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients, and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The Assessment Report shows that peginterferon alfa combination therapy is a very cost effective intervention compared with interferon alfa combination therapy. For genotype 2/3, given the very high sustained success rates at 24 weeks, treatment is cost effective at 24 weeks but not thereafter. For genotype 1, 48-week treatment is cost effective compared with stopping therapy after 24 weeks. See Table 1 in the original guideline document.

The manufacturers' models are similar in structure to that of the Assessment Report, and the estimates of cost effectiveness derived from them show even lower costs per quality-adjusted life year (QALY). In one instance, this can be explained in part by the longer time horizon (expected lifetime, as opposed to 30 years).

See Section 4.2 of the original guideline document for a detailed discussion of the cost-effectiveness analysis.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- Combination therapy with peginterferon alfa and ribavirin is recommended within its licensed indications for the treatment of people aged 18 years and over with moderate to severe chronic hepatitis C (CHC), defined as histological evidence of significant scarring (fibrosis) and/or significant necrotic inflammation.
- People with moderate to severe CHC are suitable for treatment if they have:
    - not previously been treated with interferon alfa or peginterferon alfa, or
    - been treated previously with interferon alfa (as monotherapy or in combination therapy), and/or
    - previously received peginterferon alfa monotherapy only and responded at the end of treatment but subsequently relapsed, or did not respond at the end of treatment.
- People currently being treated with interferon alfa, either as combination therapy or monotherapy, may be switched to the corresponding therapy with peginterferon alfa.
- Treatment for the groups identified in the first two recommendations (see above) should be as follows.
    - People infected with hepatitis C virus (HCV) of genotype 2 and/or 3 should be treated for 24 weeks.
    - For people infected with HCV of genotype 1, 4, 5 or 6, initial treatment should be for 12 weeks. Only people showing, at 12 weeks, a reduction in viral load to less than 1% of its level at the start of treatment (at least a 2-log reduction, see Section 4.1.2.5 of the original guideline document) should continue treatment until 48 weeks. For people in whom viral load at 12 weeks exceeds 1% of its level at the start of treatment, treatment should be discontinued.
    - People infected with more than one genotype that includes one or more of genotypes 1, 4, 5, or 6 should be treated as for genotype 1.
- People satisfying the conditions in the first two recommendations (see above) but for whom ribavirin is contraindicated or is not tolerated should be treated with peginterferon alfa monotherapy. Regardless of genotype, individuals should be tested for viral load at 12 weeks, and if the viral load has reduced to less than 1% of its level at the start of treatment, treatment should be continued for a total of 48 weeks. If viral load has not fallen to this extent, treatment should stop at 12 weeks.
- People for whom liver biopsy poses a substantial risk (such as those with haemophilia, or those who have experienced an adverse event after undergoing a previous liver biopsy), and people with symptoms of extra-hepatic HCV infection sufficient to impair quality of life, may be treated on clinical grounds without prior histological classification.
- There is insufficient evidence to recommend combination therapy using peginterferon alfa or interferon alfa in people who:
    - have previously been treated with combination therapy using peginterferon alfa, and/or
    - are younger than 18 years of age, and/or
    - have had a liver transplantation. Treatment of CHC recurrence after liver transplantation (whether or not the person had been treated with

interferon alfa or peginterferon alfa therapy at any time before transplantation) should be considered as experimental and carried out only in the context of a clinical trial.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations for clinical effectiveness are based on the results of six published randomized controlled trials.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate treatment for people with chronic hepatitis C may clear hepatitis C virus for at least 6 months after treatment cessation, improve quality of life for patients, and reduce the risk of cirrhosis and hepatocellular carcinoma.

POTENTIAL HARMS

- Many, but not all, people find interferon alfa therapy very hard to tolerate. After each injection, they may suffer influenza-like symptoms, and up to one-half of all people treated suffer from fatigue, headaches, pyrexia (fever), myalgia (aches and pains), insomnia and/or nausea. About one-quarter suffer hair loss, arthralgia (pain in the joints), rigors, irritability, pruritus (itching), depression, dermatitis and/or decreased appetite.
- Ribavirin may also cause haemolytic anaemia, for which close monitoring is required and a reduction in dose or cessation of treatment may be necessary.
- Adverse effects related to combination therapy are similar in type and frequency to those of interferon alfa monotherapy.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Ribavirin is contraindicated in pregnancy and breastfeeding, in severe debilitating medical conditions (particularly of the heart, blood, kidneys and liver), in haemoglobinopathies and in the presence of autoimmune diseases or severe psychiatric conditions.
- In pregnant or breastfeeding women, treatment with peginterferon alfa is contraindicated.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Health professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation and Audit

- Treatment for chronic hepatitis C (CHC) should be provided by physicians who are expert and experienced in the diagnosis and management of viral hepatitis, and a clinical nurse specialist for hepatitis with access to supportive services including an accredited virology laboratory, a liver pathologist and a radiology department, consistent with Department of Health (2002) Hepatitis C Strategy for England. London: Department of Health.
- All clinicians who care for people with CHC should review their current practice and policies to take account of the guidance.
- Local guidelines, protocols or care pathways that refer to the care of people with CHC should incorporate the guidance.
- To measure compliance locally with the guidance, the following criteria could be used. Further details on suggestions for audit are presented in Appendix C of the original guideline document.
    - An individual with moderate to severe CHC who is aged 18 years or older (except a woman who is pregnant or breastfeeding) is treated with peginterferon alfa and ribavirin combination therapy within licensed indications if he or she meets any one of the following.
        - The individual has not previously been treated with interferon alfa or peginterferon alfa.
        - The individual has been treated previously or is currently being treated with interferon alfa as monotherapy or combination therapy.
        - The individual has been previously treated with peginterferon alfa monotherapy only, and either responded at the end of treatment but subsequently relapsed, or was not responding at the end of treatment.
    - For an individual who meets the criteria as described above, treatment is carried out as follows.
        - If the individual is infected with hepatitis C virus (HCV) of genotypes 2 and/or 3, treatment is for 24 weeks.
        - If the individual is infected with HCV of genotypes 1, 4, 5 or 6, (or infected with more than one genotype including at least one of genotypes 1, 4, 5 or 6), initial treatment is for 12 weeks. If the viral load has been reduced to less than 1% of its level at

the start of treatment, treatment is continued for 48 weeks. If the viral load exceeds 1% of its level at the start of treatment, treatment is discontinued.

- An individual with moderate to severe CHC who is aged 18 years or older (except a woman who is pregnant or breastfeeding) for whom ribavirin is contraindicated or is not tolerated is treated with peginterferon alfa monotherapy. The individual is tested for viral load at 12 weeks of treatment. If the viral load has reduced to less than 1% of its level at the start of treatment, treatment continues for a total of 48 weeks. If the viral load has not fallen to less than 1% of its level at the start of treatment, treatment is stopped at 12 weeks.
- Before treatment is given, an individual has a liver biopsy to determine if the individual has moderate or severe CHC, except if the individual meets one of the following.
    - Liver biopsy poses a substantial risk to the individual.
    - The individual has symptoms of extra-hepatic HCV infection sufficient to impair quality of life.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of chronic hepatitis C. London (UK): National Institute for Clinical Excellence (NICE); 2004 Jan. 38 p. (Technology appraisal; no. 75).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Jan

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Dr Jane Adam, Radiologist, St George's Hospital, London; Dr Sunil Angris, General Practitioner, Waterhouses Medical Practice, Staffordshire; Dr Darren Ashcroft, Senior Clinical Lecturer, School of Pharmacy and Pharmaceutical Sciences, University of Manchester; Professor David Barnett (Chair), Professor of Clinical Pharmacology, University of Leicester; Dr Peter Barry, Consultant in Paediatric Intensive Care, Leicester Royal Infirmary; Professor John Brazier, Health Economist, University of Sheffield; Professor John Cairns, Professor of Health Economics, Health Economics Research Unit, University of Aberdeen; Professor Mike Campbell, Statistician, Institute of General Practice & Primary Care, Sheffield; Dr Mark Chakravarty, Head of Government Affairs and NHS Policy, Procter and Gamble Pharmaceuticals (UK) Ltd, Egham, Surrey; Dr Peter I Clark, Consultant Medical Oncologist, Clatterbridge Centre for Oncology, Wirral, Merseyside; Dr Mike Davies, Consultant Physician, University Department of Medicine & Metabolism, Manchester Royal Infirmary; Professor Jack Dowie, Health Economist, London School of Hygiene; Dr Paul Ewings, Statistician, Taunton & Somerset NHS Trust, Taunton; Ms Sally Gooch, Director of Nursing, Mid-Essex Hospital Services NHS Trust, Chelmsford; Professor Robert Kerwin, Professor of Psychiatry and Clinical Pharmacology, Institute of Psychiatry, London; Dr Stephen Saltissi, Consultant Cardiologist, Royal Liverpool University Hospital; Mr Miles Scott, Chief Executive, Harrogate Health Care NHS Trust; Professor Andrew Stevens (Vice-Chair), Professor of Public Health, University of Birmingham; Professor Mary Watkins, Professor of Nursing, University of Plymouth; Dr Norman Waugh, Department of Public Health, University of Aberdeen

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of chronic hepatitis C. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2004 Jan. 2 p. (Technology appraisal 75). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Pegylated interferon alpha 2a and 2b in combination with ribavirin in the treatment of chronic hepatitis C: a systematic review. Assessment report. Southampton Health Technology Assessment Centre (SHTAC), Wessex Institute for Health Research and Development; 2002 Jul. 169 p. Available in Portable Document Format (PDF) from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N0427. 11 Strand, London, WC2N 5HR.

Additionally, Audit Criteria can be found in Appendix C of the original guideline document.

PATIENT RESOURCES

The following is available:

- The use of interferon alfa, peginterferon alfa and ribavirin for the treatment of chronic hepatitis C. Understanding NICE guidance - information for people with chronic hepatitis C, their families and carers, and the public. London (UK): National Institute for Health and Clinical Excellence (NICE); 2004 Jan. 12 p. (Technology appraisal 75).

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the Department of Health Publications Order Line 0870 1555 455. ref: N0370. 11 Strand, London, WC2N 5HR.

has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on March 9, 2006.

The National Institute for Health and Clinical Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include summaries of their Technology Appraisal guidance with the intention of disseminating and facilitating the implementation of that guidance. NICE has not verified this content to confirm that it accurately reflects the original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE technology appraisal guidance is prepared in relation to the National Health Service in England and Wales. NICE has not been involved in the development or adaptation of NICE guidance for use in any other country. The full versions of all NICE guidance can be found at www.nice.org.uk.

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx.

NGC, AHRQ, and its contractor ECRI make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 10/2/2006